



RESPONSE UNDER 37 CFR 1.116-  
EXPEDITED PROCEDURE EXAMINING  
GROUP 1626

DOCKET NO: 240427US0X

**IN THE UNITED STATES PATENT & TRADEMARK OFFICE**

IN RE APPLICATION OF :  
KAI ROSSEN, ET AL. : EXAMINER: SOLOLA, T. A.  
SERIAL NO: 10/663,798 :  
FILED: SEPTEMBER 17, 2003 : GROUP ART UNIT: 1626  
FOR: METHOD OF PRODUCING 5- :  
FORMYL-2-FURYLBORONIC ACID :

**PRE-APPEAL BRIEF REQUEST FOR REVIEW**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450  
Sir:

Applicant requests review of the final rejection in the above-identified application.  
No amendments are being filed with this request.

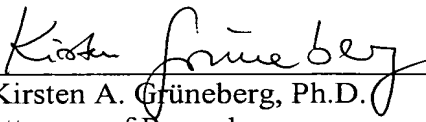
This request is being filed with a Notice of Appeal.

The review is requested for the reason(s) stated on the attached sheet(s). No more  
than five (5) pages are provided.

I am the attorney or agent of record.

Respectfully submitted,

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ATTACHMENT TO PRE-APPEAL BRIEF REQUEST FOR REVIEW

The present invention as set forth in **amended Claim 1** relates to a method of producing 5-formyl-2-furylboronic acid, comprising:

- a) reacting the formyl group of 2-furaldehyde with a protective group, to obtain a protected 2-furaldehyde;
- b) adding a base to a composition comprising a boric acid ester and said protected 2-furaldehyde, thereby obtaining a reaction mixture and reacting said protected 2-furaldehyde, said base and said boric acid ester;
- c) adding said reaction mixture to an acidic medium; and
- d) obtaining 5-formyl-2-furylboronic acid from said acidic medium.

**Claims 1-5, 7, 8 and 10-20 depend on Claim 1.**

**Claim 21** relates to a method of producing 5-formyl-2-furylboronic acid, comprising:

- a) reacting the formyl group of 2-furaldehyde with a protective group, to obtain a protected 2-furaldehyde;
  - b) adding a base to a composition comprising a boric acid ester and said protected 2-furaldehyde, thereby obtaining a reaction mixture and reacting said protected 2-furaldehyde, said base and said boric acid ester;
  - c) adding said reaction mixture to an acidic medium; and
  - d) obtaining 5-formyl-2-furylboronic acid from said acidic medium;
- wherein said base is selected from the group consisting of lithium hexamethyldisilazane, sodium hexamethyldisilazane, potassium hexamethyldisilazane, lithium diisopropylamide, butyl lithium, methyl lithium, ethyl lithium, propyl lithium, and mixtures thereof.

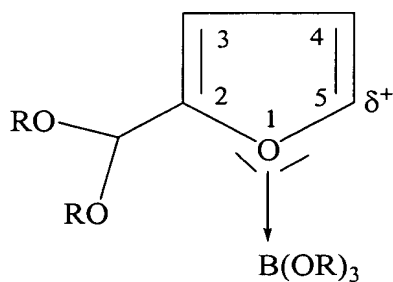
Applicants respectfully request pre-appeal review of the following issues:

1) Obviousness rejection. Claims 1-5, 7, 8 and 10-21 were rejected under 35 U.S.C. 103 (a) over Guerry et al (WO 96/16046).

Guerry et al (WO 96/16046) fail to disclose or suggest obtaining a protected 2-furaldehyde and adding a base to a composition comprising a boric acid ester and said protected 2-furaldehyde. This has been acknowledged by the Examiner. See page 5 of the Office Action.

Guerry et al is discussed in the specification at page 2, starting at line 3. The process of the **reference** has a **low yield of 26%**. It was an object of the present invention to provide a method of producing 5-formyl-2-furylboronic acid with high yield. The process of the **present invention** has **high yields of 75% and 90%** as shown in the Examples (specification at pages 7 and 8). This is a **difference of a factor of at least 3**. The order of adding the starting materials is a reason for this difference. It was not obvious based on Guerry et al to change the order of adding the starting materials. It was also not expected based on Guerry et al to obtain much higher yields by changing the order of the starting materials. In fact, a person of ordinary skill in the art would not have expected that the reaction route of the present invention could be successful.

In Guerry et al, boronic acid ester is added to a mixture of base and protected furaldehyde. The process based on Guerry et al has a **low yield of 26%**. In contrast, the process of the present invention has **high yields of 75% and 90%**. It was not obvious based on Guerry et al to change the order of adding the starting materials. In particular one has to bear in mind that  $B(OR)_3$  (boronic acid ester) is a strong Lewis acid which on addition to the furane will likely form an acid base complex like:



This complex may comprise a higher electrophilicity than the furane itself. Accordingly, it was a **surprise** that no addition of the anion of the base may occur in 5-position of the complex, but rather a deprotonation in 5-position predominantly happens, which in turn leads to the reaction with the boronic acid ester to form the desired product.

In addition, a person of ordinary skill in the art would not have expected that the reaction route of the present invention could be successful. **This is because the more reactants are present in a mixture the more side-reactions can take place.**

### CONCLUSION

In view of the above remarks, the Applicants respectfully request that the rejections of record be withdrawn.